

Breast cancer in women: a descriptive analysis of the national cancer database

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Summary. *Background and aim of the work:* Breast cancer is the most common cancer in women in the United States. National Cancer Database (NCDB) is one of the largest tumor databases of the United States. This study aimed to evaluate the features of breast cancer in women from a large updated database. *Methods:* We describe and analyze the frequencies and percentages of the clinical and pathological features of women diagnosed with breast cancer registered in NCDB, in a period from 2004 to 2015. *Results:* A total of 2,423,875 women were diagnosed with breast cancer between 2004 and 2015. The nationally representative analysis demonstrated that the incidence of breast cancer among women increased over the years. Upper-outer quadrant was the most frequent primary tumor site, and the intraductal carcinoma was the most frequent histology. The prevalence of breast cancer increased with age. The most frequent grade at diagnosis was grade II. Broadly, invasive characteristics were noted more frequently in younger patients. Left and right breast were affected with almost the same frequency, with a slight predominance of the left breast. The most frequent surgical treatment was a partial mastectomy. Reconstruction with implant was the most frequent choice. Post-mastectomy radiation therapy was administered in the majority of patients. *Conclusions:* To the authors' knowledge, the current study is the largest descriptive analysis to date on the clinical and pathological features of breast cancer in a population-based database. The increase in incidence over the years indicates an important need for etiologic research and innovative approaches to improve breast cancer prevention. (www.actabiomedica.it)

Key words: breast, cancer, breast neoplasms, epidemiology, NCDB, women

Introduction

Breast cancer in the United States is the most common cancer in women after skin cancer, regardless of race or ethnicity (1). The incidence rate for female breast cancer in the United States from 2010 to 2014 was 123.6 per 100000 population, and an estimated of 40920 American females will die from breast cancer in 2018 (2).

Data concerning this type of cancer is submitted to the nationally recognized National Cancer Da-

tabase (NCDB) every year (3). The NCDB - jointly sponsored by the American College of Surgeons and the American Cancer Society, is a clinical oncology database sourced from hospital registry data that are collected in more than 1500 Commission on Cancer (CoC)-accredited facilities. NCDB data are used to analyze and track patients with malignant neoplastic diseases, their treatments, and outcomes. As a result, the data represent more than 70 percent of newly diagnosed cancer cases nationwide and more than 34 million historical records (3). The purpose of this work

is to update the demographic and clinical data about breast cancer in women, meaningful to the surgeons and the scientific community.

Methods

We aimed to analyze data from the NCDB to assess the demographic and clinical characteristics of female breast cancer patients between 2004 and 2015 (3). Demographics and cancer-specific characteristics were calculated using IBM SPSS Statistics for Windows, Version 22.0 software (IBM Corp., Armonk, NY) and reported as frequencies and percentages. We included all female patients with breast cancer reported in the database.

Age of female patients was divided into three groups, as follows: ≤ 40 years, 40 to 60 years and > 60 years. The race was classified into White, Black, Asian, Native American and other races. The mean of the number of days between the date of diagnosis and the most definitive surgical procedure on the primary site was calculated. Tumor size was divided into the following groups: < 2 cm, 2-4.9 cm, and ≥ 5 cm. The tumor location was classified according to the International Classification of Diseases for Oncology, Third Edition which includes: breast upper-outer quadrant (UOQ), breast upper-inner quadrant (UIQ), breast lower-outer quadrant (LOQ), breast lower-inner quadrant (LIQ), breast central portion, breast axillary tail, breast overlapping lesion, and nipple (4). Laterality identified the side of the breast on which the reportable primary tumor originated.

Histology results were named according to the third edition of International Classification of Diseases for Oncology codes (ICD-O-3), reported by registries for cases diagnosed in 2001 and subsequently (4). We regrouped the histology types into the most meaningful types that have a higher percentage of occurrence in the database, as follows: 8343 code into 'papillary' type; 8070, 8071, 8072, 8074, 8075, 8076, 8052 codes into 'squamous' type; 8453, 8500, 8503, 8507, 8514, 8521 codes into 'intraductal' type; 8140, 8147, 8190 codes into 'adenocarcinoma' type; 8520 code into 'lobular' type; 8522, 8523, 8524, 8560, 8940 codes into 'mixed' type; 8530 code into 'inflammatory' type; 8540,

8541 and 8543 into 'Breast Paget' type; 9020 code into 'phylloides' type; other codes were grouped as 'others'.

The behavior of the breast cancer was reported as benign, borderline, in situ/carcinoma in situ and invasive. The grade was reported as follows: grade I, II, III and IV, where well differentiated (grade I) was the most like normal tissue, and undifferentiated (grade IV) was the least like normal tissue, as stated in diagnosis.

The stage was assigned depending on the pathologic stage group, when it was not reported it was assigned depending on the clinical stage group. The stage was divided into 0, I, II, III and IV, according to American Joint Committee on Cancer (AJCC) 7th edition traditional stage classification. We did not consider patients with not applicable or unknown stage.

The records of the surgical procedure performed in the primary site were divided into no surgery, partial mastectomy, complete mastectomy, and unknown; other kinds of procedures were excluded. The complete mastectomy group included total mastectomy, subcutaneous mastectomy, modified radical mastectomy, radical mastectomy, extended radical mastectomy, bilateral mastectomy for a single tumor involving both breasts and mastectomy NOS (not otherwise specified). Types of reconstruction after complete mastectomy were divided into reconstruction with autologous tissue, with implant and combined (with tissue and implant). We included only the patients that had a reported a type of reconstruction.

Radiation therapy was reported as follows: none (radiation not administered); beam radiation (x-ray, cobalt, linear accelerator, neutron beam, betatron, spray radiation, intraoperative radiation and stereotactic radiosurgery as gamma knife and

Proton beam); radioactive implants (brachytherapy, interstitial implants, molds, seeds, needles, or intracavitary applicators of radioactive materials as cesium, radium, radon, and radioactive gold); radioisotopes internal use of radioactive isotopes (iodine 131, phosphorus 32, strontium 89 and 90) administered orally, intracavitary, or by intravenous injection; combination of beam radiation with radioactive implants or radioisotopes.

Results

A total of 2423875 women were diagnosed with breast cancer between 2004 and 2015 (Table 1). The incidence of this disease among women increased over the years (Figure 1). Mean age was 60.91±13.36 (18-90 years old). 136525 female patients (5.6%) were ≤40 years old, 1065754 (44%) patients were between 40 and 60 years old, and 1221596 (50.4%) patients were >60 years old (Figure 2). The predominant race was white (2022918 patients, 84.3%), followed by black (271401 patients, 11.3%), Asian (6138 patients, 0.2%), Native American (78535 patients, 3.2%) and other (18256 patients, 0.7%). The average number of days between the date of diagnosis and the date on which the most definitive surgical procedure was performed on the primary site was 51. Concerning the size of the tumor, 31574 (1.30%) patients had a <2 cm tumor, 148008 (6.11%) patients had a tumor between 2-4.9 cm, and 2244293 (92.59%) patients had a tumor ≥5cm (Table 2).

Within this cohort, the location of the breast cancer (Figure 3) was UOQ for 807728 patients (39.50%), UIQ for 255431 patients (12.49%), LOQ for 170278 patients (8.33%), LIQ for 136025 patients (6.65%), the central portion of the breast for 124531 patients

Table 1. Demographic data

Characteristic	n	%
Total females with breast cancer	2423875	100
Age		
<=40 years old	136525	5.60%
40-60 years old	1065754	44.00%
>60 years old	1221596	50.40%
Race*		
White	2022918	84.39%
Black	271401	11.32%
Asian	6138	0.26%
Native American	78535	3.28%
Other	18256	0.76%
Period of diagnosis		
2004-2006	513042	21.17%
2007-2009	588678	24.29%
2010-2012	631994	26.07%
2013-2015	690161	28.47%

*patients with unknown race were excluded

(6.09%), the nipple for 14392 patients (0.7%), axillary tail of breast for 9972 patients (0.49%) and overlapping lesion of breast for 526593 patients (25.75%). The

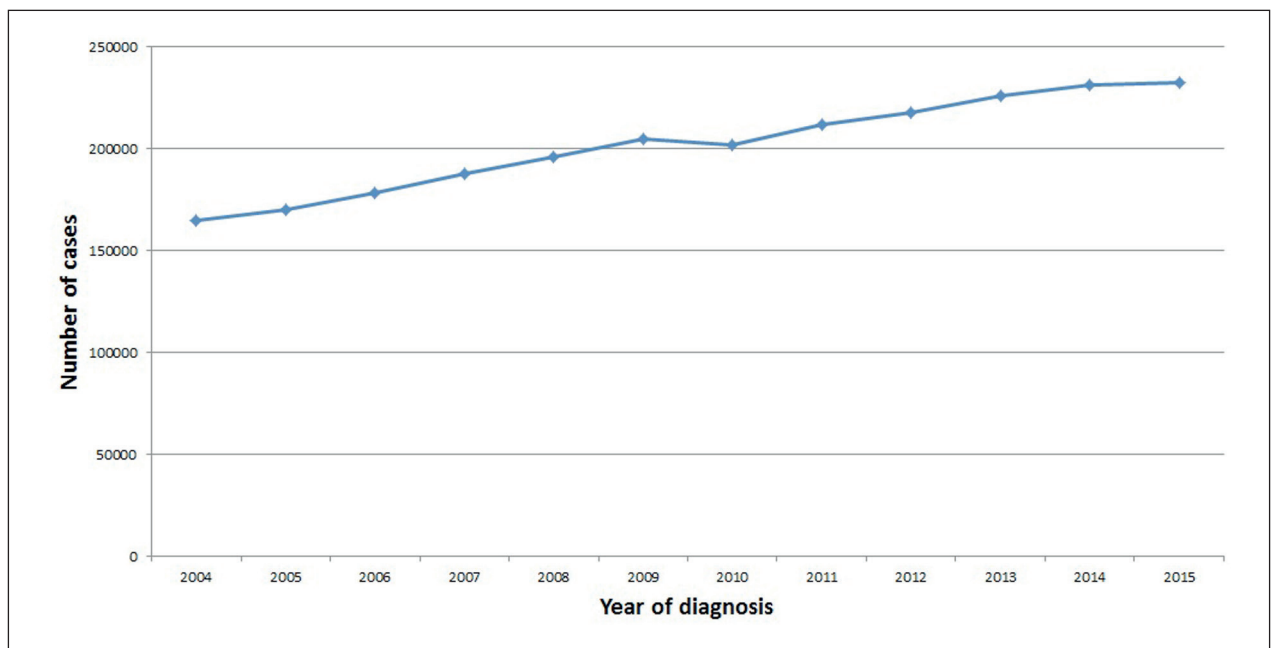


Figure 1. Number of female breast cancer cases in the United States from 2004 to 2015

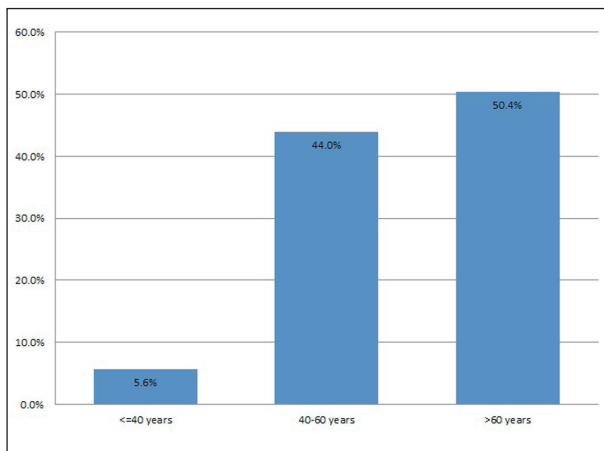


Figure 2. Age at diagnosis

primary tumor site was left breast in 50.6% of patients and the right breast in 49% of patients.

Histology results were reported (Table 2 and 3, Figure 4) as follows: 1629174 (67.21%) patients had intraductal carcinoma, 235379 (9.71%) patients had lobular carcinoma, 15073 (0.62%) patients had adenocarcinoma, 8831 (0.36%) patients had papillary carcinoma, 8277 (0.34%) patients had inflammatory carcinoma, 7087 (0.29%) patients had mammary Paget, 3227 (0.13%) patients had phylloides, 937 (0.04%) patients had squamous carcinoma, 293746 (12.12%) patients had a mixed histology between these types, and 222144 (9.16%) patients had another types of tumor on histology.

The behavior of the breast cancers was invasive for 1932688 patients (79.7%) followed by in situ/carcinoma in situ for 491187 (20.3%) patients; there was not any benign or borderline tumor included in the database. The grade as stated in the final pathologic diagnosis (Table 2, Figure 5) was I for 461096 patients (19%), II for 920687 patients (38%), III for 719178 patients (29.7%), IV for 20216 patients (0.8%), not determined for 302698 patients (12.5%). With respect to stage, 486856 (20.88%) patients corresponded to Stage 0, 961981 (41.27%) patients to Stage I, 587352 (25.20%) patients to Stage II, 203159 (8.71%) patients to Stage III, 91864 (3.94%) patients to Stage IV.

Overall, 1320210 (54.57%) patients underwent partial mastectomy, whereas 922391 (38.13%) patients underwent complete mastectomy (Table 4, Figure 6).

Table 2. Breast cancer characteristics

Characteristics of tumor	n	%
Tumor size		
<2 cm	31574	1.30%
2-4.9 cm	148008	6.11%
>=5 cm	2244293	92.59%
Primary tumor site		
Left breast	1225286	50.60%
Right breast	1188795	49.00%
Location*		
Nipple	14392	0.70%
Central portion of the breast	124531	6.09%
Upper-inner quadrant	255431	12.49%
Lower-inner quadrant	136025	6.65%
Upper-outer quadrant	807728	39.50%
Lower-outer quadrant	170278	8.33%
Axillary tail of breast	9972	0.49%
Overlapping lesion of breast	526593	25.7%
Histology types		
Papillary carcinoma	8831	0.36%
Squamous carcinoma	937	0.04%
Intraductal carcinoma	1629174	67.21%
Adenocarcinoma	15073	0.62%
Lobular carcinoma	235379	9.71%
Mixed types	293746	12.12%
Inflammatory carcinoma	8277	0.34%
Mammary Paget	7087	0.29%
Phylloides	3227	0.13%
Others	222144	9.16%
Behavior		
In situ	491187	20.30%
invasive	1932688	79.70%
Grade **		
I	461096	21.70%
II	920687	43.40%
III	719178	33.90%
IV	20216	0.95%
Stage ***		
Stage 0	486856	20.88%
Stage I	961981	41.27%
Stage II	587352	25.20%
Stage III	203159	8.71%
Stage IV	91864	3.94%

* 378925 patients with not otherwise specified location of the tumor were excluded

** 302698 patients who did not have information on grade were excluded

*** 92663 patients with unknown stage were excluded

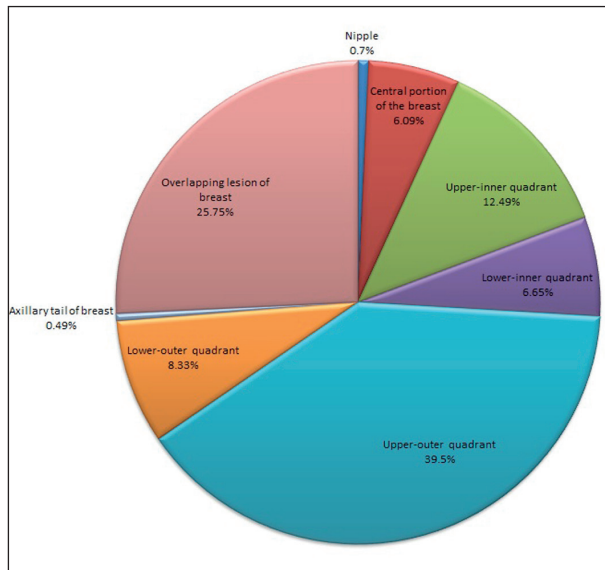


Figure 3. Location of the primary tumor

According to the type of reconstruction after complete mastectomy, 93405 (40.02%) patients underwent reconstruction with autologous tissue, 106130 (45.47%) patients underwent reconstruction with implants, and 33861 (14.51%) patients underwent combined reconstruction with tissue and implant (Table 3).

Radiation therapy was not administered in 1140676 patients (47.63%). 1165746 patients (48.67%) underwent beam radiation, 72500 patients

(3.03%) radioactive implants, 625 patients (0.03%) radioisotopes and 2462 patients (0.10%) combination of beam radiation with radioactive implants or radioisotopes (Table 3).

Radiation therapy before surgery was administered in 7967 patients (0.33%) and after surgery in 1214097 patients (50.77%). Overall thirty-day mortality was 0.1% (2200 patients), whereas overall ninety-day mortality was 0.3% (7635 patients).

Discussion

The current study is the largest descriptive analysis to date on the clinical and pathological features of breast cancer in a population-based database. Breast cancer occurs more frequently in the UOQ, and we observed an overall prevalence of 39.50% in this study. Previous studies on smaller cohorts of patients observed a prevalence of UOQ tumor location ranging from 36.1% to 62% (Table 7) (5-8, 10-12). The higher frequency of occurrence of breast cancer in the UOQ is generally attributed to the higher amount of tissue in that breast quadrant (13). Nevertheless, the larger amount of breast tissue alone in UOQ cannot completely explain the disproportional occurrence of breast cancer in each quadrant (14). Ellsworth et al. observed a greater genomic instability in outer breast

Table 3. Age distribution depending on histology

Histology	Mean age (years)	Std. Deviation	Number of patients
Papillary	68.11	12.757	8831
Squamous	64.51	14.469	937
Intraductal	60.53	13.448	1629174
Adenocarcinoma	63.44	14.064	15073
Lobular	61.92	12.867	235379
Mixed	61.13	12.931	293746
Inflammatory	57.84	13.929	8277
Angyomyosarcoma	69.38	7.999	8
Paget	63.62	14.949	7087
Phylloides	52.35	14.548	3227
Others	62.04	13.436	222136
Total	60.91	13.366	2423875

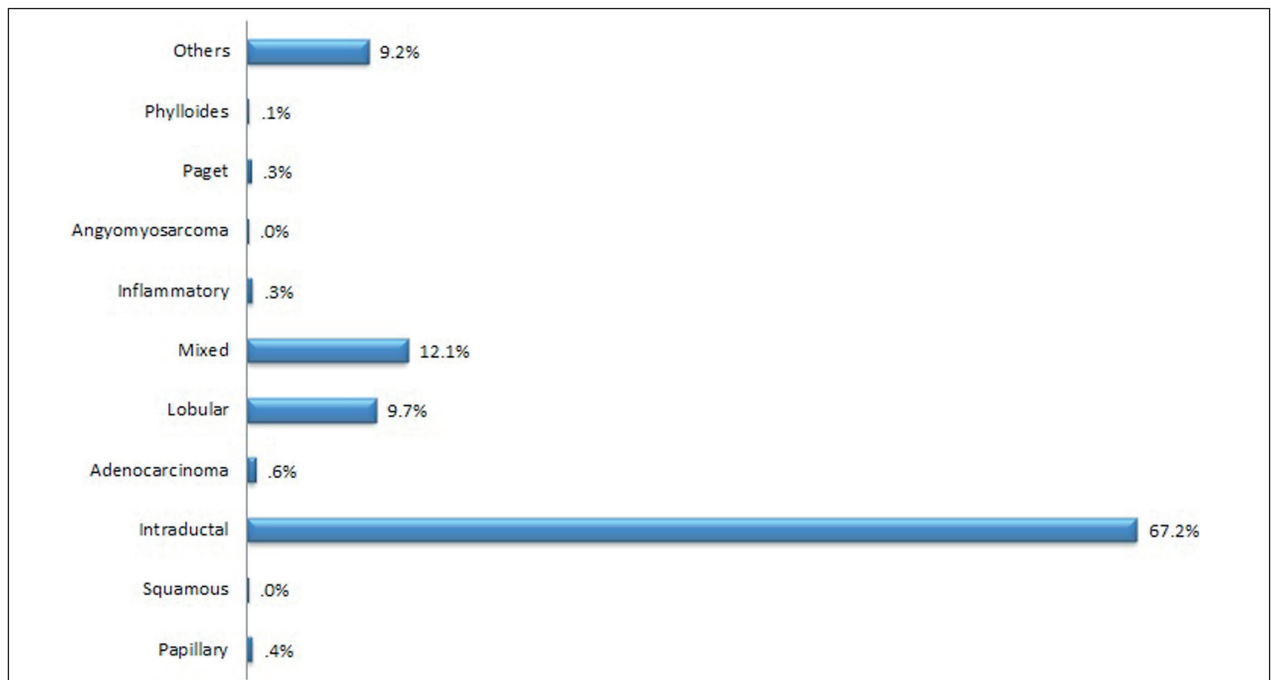


Figure 4. Histology

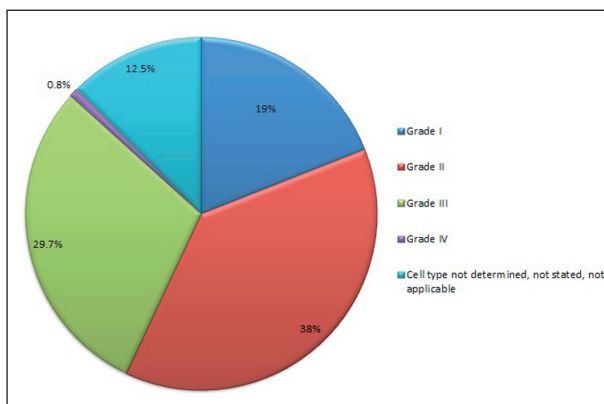


Figure 5. Grade at diagnosis

quadrants compared with the inner quadrants (15). Darbre observed that the higher occurrence of breast cancer in UOQ could be related to the use of cosmetics applied to the adjacent underarm and upper breast area, that may contain both DNA-damaging chemicals and chemicals which in turn could mimic estrogen action (16).

Our descriptive analysis of breast cancer in the United States showed that the incidence of this disease among women has increased over the years, with

exception of a sharp reduction in 2010 (Figure 1). Hou et al. already showed a significant increase in the incidence rates of all breast cancer from 2000 to 2009 (17). We confirmed the same upgoing trend from 2010 to 2015 as well. Furthermore, the prevalence of breast cancer increased with age, which Stapleton et al. also observed while studying the Surveillance, Epidemiology, and End Results (SEER) Program database (18). From our NCDB analysis, 94.4% of patients were diagnosed with breast cancer after 40 years old (44% between 40 and 60 years old and 50.4% after 60 years old). As such, annual mammography is strongly suggested after the age 40, as it is demonstrated to decrease mortality (19).

The most frequent histology type in our study was an intraductal carcinoma, followed by lobular carcinoma, in accordance with the literature data (Table 4) (20, 21). Broadly, invasive characteristics were noted more frequently in younger patients, in accordance with the findings by Escarela et al. from a SEER analysis (21). Presence of tumor cells in lymphatic channels (not lymph nodes) or blood vessels within the primary tumor was noted more frequently in younger patients, as well as a higher grade at diagnosis (Table 5 and 6).

Table 4. Management. NOS: Not otherwise specified

Treatment	n	%
Type of surgery *		
None	171966	7.11%
Local tumor destruction, NOS	352	0.01%
Partial mastectomy	1320210	54.57%
Subcutaneous mastectomy	18218	23.79%
Total (simple) mastectomy	575422	0.75%
Modified radical mastectomy	306483	12.67%
Radical mastectomy	11128	0.46%
Extended radical mastectomy	427	0.02%
Bilateral mastectomy for a single tumor involving both breasts, as for bilateral inflammatory carcinoma	288	0.01%
Mastectomy, NOS	11140	0.46%
Surgery, NOS	3481	0.14%
Type of reconstruction		
Autologous tissue	93405	40.02%
Implant	106130	45.47%
Combined (tissue and implant)	33861	14.51%
Type of radiation **		
None (Radiation not administered)	1140676	47.63%
Beam radiation	1165746	48.67%
Radioactive implants	72500	3.03%
Radioisotopes	625	0.03%
Combination of beam radiation with radioactive implants or radioisotopes	2462	0.10%
Radiation therapy NOS	13012	0.54%
Radiation sequence with surgery ***		
No radiation therapy and/or surgical procedures	1162082	48.59%
Radiation before surgery	7967	0.33%
Radiation after surgery	1214097	50.77%
Radiation before and after surgery	1009	0.04%
Intraoperative radiation	5017	0.21%

* 4760 patients who did not have information about surgery were excluded

** 28854 patients who did not have information on radiation were excluded

*** 32429 patients who did not have information on radiation sequence were excluded

The post-mastectomy reconstruction with implant was the most used reconstructive modality, whereas the reconstruction with autologous tissue and combined were less frequently performed, probably due to the cost and the necessity of suitable instruments such as the microscope (22). Moreover, disadvantages of autogenous tissue-based reconstruction

could bring to prefer the reconstruction with implants, including longer anesthesia, more blood loss, a longer hospitalization, risk of necrosis of the flap, and possible issues at the donor site (scars, and abdominal hernias) (23). The risk of complications after breast reconstruction with autologous flap increases with age and BMI (body mass index), in smokers and diabetic patients

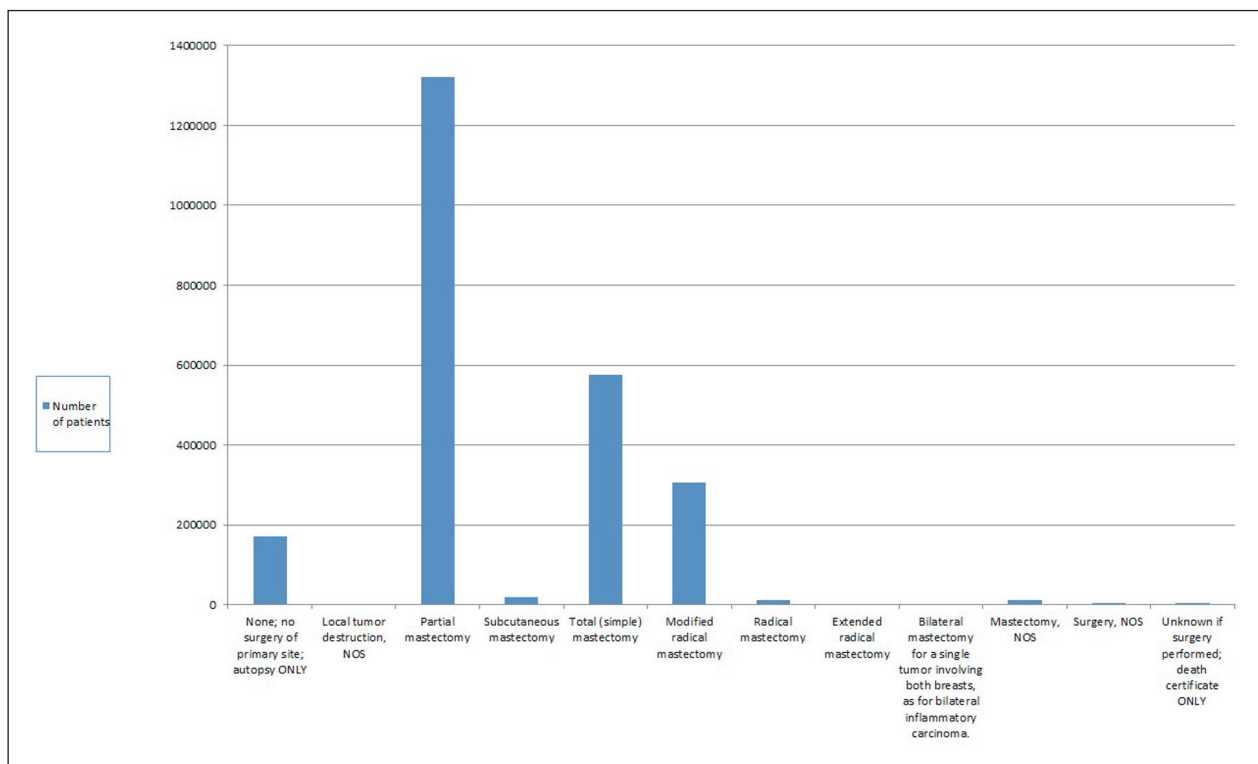


Figure 6. Type of surgery

Table 5. Age distribution depending on Grade

Grade	Mean age (years)	Std. Deviation	Number of patients
Grade I	63.29	12.589	461096
Grade II	61.80	13.238	920687
Grade III	58.53	13.632	719178
Grade IV	58.90	13.226	20216
Cell type not determined, not stated, not applicable	60.38	13.333	302698
Total	60.91	13.366	2423875

Table 6. Presence or absence of tumor cells in lymphatic channels (not lymph nodes) or blood vessels within the primary tumor as noted microscopically by the pathologist. 1101720 patients with missing data were not included

Lymph-vascular invasion	Mean age (years)	Std. Deviation	Number of patients
Lymphovascular invasion is not present	61.60	12.792	858226
Lymphovascular invasion is present	59.24	13.947	168431
Not applicable	61.57	12.898	6272
Unknown	61.25	13.588	289226
Total	60.91	13.366	2423875

Table 7. Percentage of primary breast tumor location in UOQ (upper-outer quadrant) as reported in other studies and in this study

Author, year	Location of the study	Total Number of patients included	Database analyzed	Years	UOQ tumor location (%)
Hazrah P (5)	India	187	Department Of Surgery All India Institute of Medical Sciences	1994-2005	62
Rummel S (6)	USA	980	Clinical Breast Care Project	2001-2013	51.5
Wu S (7)	China	1044	Sun Yat-Sen Cancer Center	1999-2007	50.2
Sarp S (8)	Switzerland	1522	Geneva Cancer Registry	1984 - 2002	39
Nunes RD (9)	Brazil	2582	Population-Based Cancer Registry of Goiânia (RCBPGO)	1989-2003	53.7
Siotos C (10)	USA	5295	Johns Hopkins Sidney Kimmel Comprehensive Cancer Center	2003-2015	36.2
Sohn VY (11)	USA	26,121	The Department of Defense tumor registry encompasses all military facilities from the United States Army, Air Force, and Navy	1990-2005	57
Eisemann N (12)	Germany	Not specified	Epidemiological cancer register of Schleswig-Holstein	1999-2009	36.1
Sisti A (this study)	USA	2423875	National Cancer Database (NCDB)	2004-15	39.50

(23). Post-mastectomy radiation therapy (PMRT) is generally recommended for patients with advanced disease (24). It has been shown to improve control of local disease and overall survival. There is also a reduction in relapse rates for patients with more than three positive lymph nodes. In our cohort, PMRT was administered to 1214097 patients (50.77%).

Conclusion

This nationally representative analysis of the years 2004-2015 demonstrates that UOQ was the most frequent primary tumor site and the intraductal carcinoma was the most frequent histology. The prevalence of breast cancer increased with age. The most frequent grade at diagnosis was grade II. Left and right breast were affected with almost the same frequency, with a slight predominance of the left breast. Most frequent surgical treatment was a partial mastectomy. Reconstruction with implant was the most frequent choice.

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Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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